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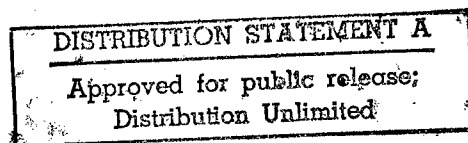
24 April 1961

CURRENT PROBLEMS OF THE PHYSIOLOGY, MORPHOLOGY, PHARMACOLOGY
AND CLINICAL PICTURE OF RETICULAR FORMATION OF THE BRAIN

-USSR-

By P. K. Anokhin and V. G. Agafonov

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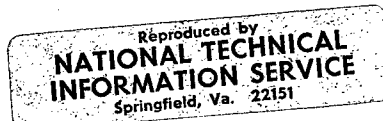
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FOREWORD

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CURRENT PROBLEMS OF THE PHYSIOLOGY, MORPHOLOGY, PHARMACOLOGY,
AND CLINICAL PICTURE OF RETICULAR FORMATION OF THE BRAIN

- USSR -

[Following is a translation of an article by P. K. Anokhin
and V. G. Agafonov, in Vestnik Akademii Meditsinskikh Nauk
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The First Combined Scientific Conference devoted to the problems of the physiology, morphology, pharmacology, and the clinical picture of the reticular formation of the brain, organized by the Institute of Normal and Pathological Physiology of the Academy of Medical Sciences USSR, the Moscow Physiological Society, and the First Moscow Order of Lenin Medical Institute imeni I. M. Sechenov, was held in Moscow in March 1960. Over 500 scientists and physicians of various calibers and branches took part in the work of the conference; more than 70 scientific communications from 12 cities of the Soviet Union were delivered. At the conclusion of the work of the conference the directors of laboratories occupied by the study of this problem held a special symposium in which the work of the conference was summed up, and the prospects and the course of further investigations concerning the relationship between the cortex and the subcortex were tentatively planned.

The work of the conference opened with a series of introductory papers.

In the paper of Member of the Academy of Medical Sciences USSR, Prof P. K. Anokhin, entitled "The Present Concept of the Role of the Reticular Formation in the Integrating Activity of the Brain", the basic principles of the physiology of the reticular formation which had been established as a result of the analytical investigations of Western scientists, were subjected to critical discussion. Firstly, the question was posed as to the correctness of the concept which has been widely accepted by the world's neurophysiology, namely, that the activating influence of the reticular formation on the brain cortex is "non-specific". As indicated by the experiments of the speaker and a number of his associates, this concept completely disregards the unique and specific character of the effects which the brain cortex and the reticular formation exert on one another in the process of the development of conditionally-reflective relationships which are biologically opposed to each other in their signs (defensive and alimentary conditioned reflexes).

It has been found that each one of these different states of the animal is characterized by its own specific activating influence exerted by the reticular formation on the cortex of the cerebral hemispheres.

Another point which was analyzed in detail in the paper pertained to the problem of the internal organization of the reticular formation. On the basis of a number of experimental data a new concept of the functional heterogeneity (non-uniformity) of the reticular formations has been developed. Let us recall the fact that even now the majority of foreign scientists continue to regard the reticular formation as an accumulation of homogeneous and functionally non-specific groups of neurons. According to the data of the speaker and his associates such a concept is one-sided and does not reflect the abundance of functional relations and combinations thereof existing in the reticular formation. Interesting and illustrative evidence of the correctness of the theses proposed by the speaker is supplied by the experiments on the analysis of subcortical tracts of the so-called "secondary" bio-electric responses in the cortex of the cerebral hemispheres and the study of these tracts and their mechanics in postnatal ontogeny, and also of the selective action of a number of chemical substances on neuron groups of the reticular formation.

The last problem posed by the speaker concerned the role and significance of the method of conditional reflexes in the study and comprehension of the analyzing-synthesizing activity of the brain. In this section of the report, the author emphasized the leading role of the cortex of the cerebral hemispheres in establishing and strengthening the temporary connections and rigorously criticized the attempts of individual foreign scientists to ascribe the principal role in the closing of the arc of the conditioned reflex to the reticular formation.

The second introductory paper heard at the opening of the conference was the communication of Member of the Academy of Medical Sciences of the USSR, Prof S. A. Sarkisov, entitled "Once Again on the Center of Sleep on the Basis of Data on the Reticular Formation." In his paper S. A. Sarkisov dwells in detail on the analysis of the latest experiments of Prof D. Morruksi [Russian transliteration] and his associates on the subject of the existence of synchronizing mechanisms in the caudal regions of the reticular formation of the medulla oblongata; the activation of these mechanisms is associated with generalized synchronization, the electroencephalogram and the development of sleep. Following up on these new facts, the speaker posed the question of the relationship between these synchronizing systems of the medulla oblongata with the well-known hypothalamic sleep center and the cerebral cortex. S. A. Sarkisov assumes that the synchronizing apparatuses of the reticular formation constitute only one of the elements of the complex cortical-subcortical system of the mechanics of the development of sleep, whereas the hypothalamic center plays the role of an important intermediate phase between the cerebral cortex and the synchronizing apparatus of the caudal regions of the medulla oblongata. The connections between the cerebral cortex and, especially, its frontal regions, and the hypothalamus are an

accepted fact in the morphological and physiological literature. At the same time there are virtually no indication of the existence of a connection between the hypothalamic nuclei and the caudal regions of the reticular formation. S. A. Sarkisov adduced pertinent data on the existence of a mammo-segmentary descending bundle terminating exactly in the area of the pons varolii wherein, according to D. Marrutsi's data, the synchronizing apparatuses of the reticular formation are localized. In the opinion of S. A. Sarkisov, these descending bonds are the bonds which establish the connection between the cerebral cortex, the hypothalamic sleep center, and the synchronizing system of the lower regions of the medulla oblongata.

The second problem discussed in the paper referred to the experimental verification of the experiments of Lindeli, Megun, and their associates who demonstrated the significance of the rostral regions of the reticular formation in the change between the states of sleep and wakefulness. Prof S. A. Sarkisov and his associates, upon performing continuous experiments on monkeys by destroying the reticular formation of the midbrain (with subsequent histological control of the points of the destruction) did not verify the data of Lindeli and Megun. The selective destruction of the above indicated regions of the reticular formations performed in S. A. Sarkisov's experiments did not disrupt the normal course of the "wakefulness--sleep" cycle in the monkeys operated upon.

The third comprehensive communication on the subject of the "Cortical Regulation of the Activity of the Non-specific Formations of the Brain" was given by Prof S. P. Narikashvili (Institute of Physiology of the Academy of Sciences Georgian SSR, Tbilisi). In his report S. P. Narikashvili summarized and adduced the data on the reverse regulating effect exercised by the cerebral cortex on the activity of the reticular formations of the medulla oblongata and the thalamus. The speaker reiterated that an absolute majority of investigators working in this area studied mainly the ascending effects of the reticular formation, and this fact brought about a number of important and interesting discoveries in this area. At the same time a concept was formulated on the dominant role of the reticular formation in a great number of important problems, such as the regulation of the flow of sensory stimuli along the specific tracts and the development of the "habituation." S. P. Narikashvili adduced a number of conclusive data which indicate the leading role played by the cerebral cortex in the development of the "habituation" phenomena in the control of the activity of the diffusive projectional system of the thalamus and the reticular formation of the medulla oblongata. On the basis of the experiments of F. Bremer and his associates the speaker showed the leading role of the cerebral cortex in the development of the reaction of awakening. In S. P. Narikashvili's opinion the cerebral cortex is also highly active in the regulation of the flow of affecting stimuli, which enter the central nervous system along the classical tracts. In conclusion the speaker examined and criticized the attempts of individual foreign investigators to ascribe the leading role in the closing of the temporary connection to the reticular formation and to

localize therein a number of higher psychic functions of man.

The subsequent work of the conference proceeded in plenary sectional meetings devoted to the following subjects: "The Morphology of the Reticular Formation," "The Physiology of the Reticular Formation," "The Problem of the Ontogeny and the Neurochemical Sensitivity of the Reticular Formation," "The Reticular Formation and the Physiology of the Higher Nervous Activity," "Adrenalin, the Sympathetic Tonus, and the Reticular Formation," "The Internal Medium of the Organism, Interoception and Their Connection with the Reticular Formation," "Clinical and Experimental Pathology and the Reticular Formation."

The present communication is confined to the examination of individual communications manifesting the greatest interest in the over-all consecutive thematic order of the sessions.

1. Morphology of the Reticular Formation

One of the most interesting problems discussed at the conference was that of the morphology of the reticular formation. Of the eight reports heard during this session, the following proved to be of greatest interest: the paper by G. P. Zhukova and T. A. Leontovich (Moscow) "On the Unique Features of the Structure and Connections of the Reticular Formation," and S. B. Dzugayeva's (Moscow) address "The Anatomy of the Reticular Formation and the Conducting Tracts of the Brain During the Process of Evolution."

The report of G. P. Zhukova and T. A. Leontovich presented interesting materials pertaining to the fine neuron structure of the reticular formation which distinguishes it from the structure of the neurons of the "specific" formations. On the basis of the above data, the authors attempted to describe the topography of the reticular formation in the spinal cord and the brain and also compiled a survey of the conducting tracts and structures classified by the authors as the reticular formation and their afferentation from the various analyzers. The comparative study by the Gol'dzhi method of the "Specific" and the reticular formation showed that the latter is characterized by a special structure of the neurons differing from those found in the specific formations. The differences discovered in the structures of the reticular and specific neurons permitted the authors to adapt the shape of the neurons as a histological criterion for judging whether a certain formation can be classified as reticular.

Basing themselves on their investigations the speakers are of the opinion that the peculiar features of the structure of the reticular formation neurons and the character of its connections point to the closest relationship of the reticular formation to the vegetative functions of the organism and to its integrating role at the level of the spinal cord, medulla oblongata and the phylogenically ancient regions of the midbrain and the cerebrum.

Interesting data on the general principles of the development of the reticular formation and the conducting tracts in the process of

evolution were presented in the paper of S. B. Dzugayeva. Upon comparison of the phylogenically ancient portions of the brain, to which the reticular formation belongs, with the development of the phylogenically recent formations, the speaker showed that in the process of the phylo- and ontogenic development the reticular formation undergoes changes which lead to a decrease of its significance in the higher stages of phylogenesis. S. B. Dzugayeva is of the opinion that among the animals the existence of a well developed reticular formation creates wider possibilities for the transfer of stimuli from one analyzer to the other within the boundaries of the medulla oblongata. In man these possibilities are represented more widely and with greater variations in the cerebral hemispheres owing to the existence of well developed projectional, commissural, and associative tracts.

The paper read by V. V. Amunts (Moscow) was also devoted to the problem of the development of the reticular formation of the medulla oblongata in a number of mammals. She showed the transformation of the cellular elements of the reticular formation from the simple to the complex forms in the process of phylogenic development.

In the paper by N. N. Bogolepov (Moscow) data were adduced on the ontogenic development of the reticular formation in man.

The important problem of the analysis of the ascending connections of the spinal cord and the reticular formation was treated in the paper by N. K. Totibadze (Tbilisi); the analysis was executed by the delicate morphological method of Naut Gigaks. P. Z. Berlin (Moscow) presented a histo-chemical investigation of the action of chlorpromazine on the reticular formation of the medulla oblongata.

In summing up the morphological investigations reported at the conference we can state that certain achievements exist in this aspect of the study of the reticular formation. The fine methods employed and the profound analysis of the factual data in the papers delivered render these papers equal to the best works of the foreign authors. However, the defects which had become apparent must also be mentioned. This applies chiefly to the absence of a broad contact between the morphological and physiological investigations of the reticular formation. This specific shortcoming was pointed out by most of the persons who had taken part in the discussions. In this respect our morphological investigations are inferior to the best works of the foreign scientists, as for example, the neurohistologists A. and M. Scheib, who work in close contact with neurophysiologists.

2. Physiology of the Reticular Formation

In this section we cannot dwell in detail on all the 12 papers delivered at the session of the conference. Therefore, we shall give only a short characteristic of the principal scientific trends of the communications here.

The paper of Prof F. N. Serkov and his associates (Odessa) presented data on electrical activity of various regions of reticular formation. For the solution of this problem the speaker and his associates successfully employed the method of cutting across the medulla oblongata at various levels. They had demonstrated the existence of explosive electrical activity as a special type of activity specific to the activity of the reticular formation only.

The data on the effect of the cortex of the cerebral hemispheres on the function of the thalamic non-specific nuclei were presented in the papers of Prof S. P. Narikashvili and his associates. In particular, they showed that upon the stimulation of the sensor-motor zone of the cortex the "involving reaction" changes considerably, which fact is exposed in the prolonged suppression of the increasing phase. The facts obtained by them provide the basis for regarding the reticular formation as an intermediate formation through which the cerebral cortex exercises its control on the other subcortical formations.

Papers from the laboratory of P. K. Anokhin were devoted to the analysis of the ascending influences of the reticular formation and to the characteristics of its functional heterogeneity. M. M. Bantsekina presented materials on the characteristics of the so-called "adjusted" rhythms (4-6 per second) in various regions of the cerebral cortex of the rabbit, which arise initially in the reticular formation. The speaker demonstrated interesting facts which indicate a sharp differentiation between the bioelectrical rhythms in the cortex of the cerebral hemispheres and in the subcortical areas. A number of examples adduced in the papers of V. A. Polyantsev and V. G. Agafonov attests to the peculiar properties of the functional heterogeneity of the reticular formation.

L. A. Novikova (Moscow) described the role of the specific and non-specific afferent systems in upholding the level of the excitability of the cortex. By working with animals with deafferent optical analyzer and registering the electrical activity of various cortical and subcortical areas, she showed that the optical deafferentation causes a depression of electrical activity and a retardation of cortical rhythm in the senso-motor area also, and not only in the occipital area of the cortex. Simultaneously we observe an increase in the thresholds of the motor reactions upon the excitation of the senso-motor area. The author draws the conclusion that the excitation level and the character of the cortical rhythm of the senso-motor area in the presence of optical deafferentation is determined by intercortical effects expanding over the cortex and not by the subcortical effects of the reticular formation.

The data on the existence of synchronizing mechanisms in the caudal sections of the reticular formations of the medulla oblongata of cat and man were presented in papers by R. F. Makul'kin (Odessa) and I. M. Gil'man (Moscow).

In reviewing the physiological papers heard at the conference we must point out that during the recent years the number of investigations in this important area increased appreciably. However, we must note that the papers contained virtually no electrophysiological data on the fine characteristics of neurons of the reticular formation

obtained through the use of the micro-electrode technique of investigation and there were too few communications describing the regulating effect of the cerebral cortex on the activities of reticular formations of the medulla oblongata and the thalamus.

3. The Problem of the Ontogeny and the Neurochemical Sensitivity of the Reticular Formation

The paper by Prof A. A. Volokhov and associates (Moscow) presented a great number of materials on the formation and development of the reticular formation of the medulla oblongata in ontogeny. These materials discussed the effect of the reticular formation on the reciprocal relationships of the antagonist muscles of the caudal extremities, on the electrical activity of the cortex of the cerebral hemispheres, and on the relationship between the somatic and the vegetative components of the conditional defensive reflex in animals in ontogeny. A. A. Volokhov draws the conclusion on the basis of the investigations performed that the formation and development of the activating portion of the reticular formation of the medulla oblongata passes through separate phases in ontogeny.

A number of important facts were reported by Prof I. A. Arshavskiy (Moscow). His paper covered the effect of the reticular formation on the specific character of the development of sleep and narcosis during different age periods. In addition to this the paper of I. A. Arshavskiy touched upon several general theoretical problems related to the mechanics of the accomplishment of central inhibition which is the basis of natural sleep and narcosis.

New and extremely interesting factual material was presented in the paper by F. A. Ata-Muradova.

The correlation of physiological observations with the morphogeny of the structural relationships between the cortex and subcortical formations caused F. A. Ata-Muradova to assume that the characteristic changes in the electrical activity of the brain during the early postnatal period are the result of heterochronic maturing of different nerve formations of the cortex and the subcortex. On the basis of these considerations the author initiated fine investigations with the analysis of individual components of the response produced in the cortex of newborn rabbits. The speaker also established the fact that immediately upon birth a single stimulation of the sciatic nerve produces only the negative form of the primary cortical response. This initial fragment of the potential produced is manifested in a limited point of the senso-motor cortex. Towards the end of the first week the true primary response appears almost simultaneously with the positive phase of the primary response. The dissimilar evolution of these fragments of the cortical potential produced is, in the author's opinion, an indicator of the difference of the ascending tracts, conducting the afferent excitation in the cerebral cortex.

Interesting comparative-physiological data on the ascending activating effect of the reticular formation were presented in the paper

by V. I. Gusel'nikov (Moscow).

We must note that foreign authors are conducting virtually no analogous investigations on the study of the development of various functions of the reticular formation in the ontogeny. Only in the most recent time isolated communications began to appear in the literature, such as those from Sherer's [transliterated from Russian] laboratory (Paris).

The second problem discussed during this session concerned the neurochemical sensitivity of the reticular formation.

A. V. Val'dman (Leningrad) presented abundant material on the effect of pharmacological substances on the somatic and vegetative functions of the reticular formation. He showed that the pharmacological experiment discloses unequal sensitivity of the neurons of the reticular formation to certain substances. Thus, various analgesics depress to varying degrees the development of the reaction of the activation of the encephalogram. Descending, inhibiting, and facilitating effects which are similar in their physiological characteristics and affect the reflexes of the spinal cord, were obtained in an experiment upon the stimulation of a 2-3 different areas of the reticular formation and were depressed in different ways by the neurotropic substances. The speaker assumes that this is caused, in particular, by the dissimilar topography of the choline- and adreno-reactive systems in the reticular formation. A. N. Val'dman comes to the conclusion that the abundance of various neurons and synapses of the reticular formations which differ morphologically and biochemically creates unlimited possibilities for discovering substances which are able to affect selectively the course of the nervous stimulation, and, consequently, to depress or augment certain somatic or vegetative functions of the reticular formation.

The paper by Liu Chuan-kuei (P. K. Anokhin's laboratory, Moscow) adduces new factual materials on the existence of an "urethan" secondary response in the cerebral cortex, which is different from the "classical" secondary response, described by Forbes and Morrison in 1939. Using the urethan narcosis and recording the potentials produced in the cerebral cortex in response to a single stimulation of the sciatic nerve the speaker succeeded in recording a generalized positive non-primary response with a latent period of 50-70 m/sec, which had not been previously described by other authors.

On the basis of the analysis of the materials of the histological control the author believes that the secondary response studied by him is related to the subthalamus and that the collaterals leading to the latter diverge from the lemniscal system above the corpora quadrigemina.

P. P. Danisenko's (Leningrad) data on the relationship between the structure of the central cholinolithics and their action on the ascending activating system of the reticular formation of the brain are related in a similar manner to the selective chemical activity of the neurons of the reticular formation.

4. The Reticular Formation and the Physiology of the Higher Nervous Activity

The principal papers heard at this session were the communications of Prof L. G. Trofimov (Moscow) and A. I. Shumilina (Moscow).

L. G. Trofimov and N. N. Lubimov reported on the functional relationships of the cerebral cortex and the reticular formation upon action of various stimulants. Performing a continuous experiment on a dog and using a simultaneous recording of the electric potentials of various structures of the cerebral cortex, the nonspecific nuclei of the thalamus (the parafascicular complex) and the reticular formation they observed that under the action of external stimulations (light, sound) along with the parallel-proceeding variations of the electrical activity of the above mentioned formations in the presence of a sharply expressed desynchronization reaction in the cortex an insignificant change or inhibition of the electrical activity in the structures of the reticular formation frequently exists. At the same time the potentials produced, which correspond to the rhythm of the stimulation are noted in the corresponding projection zone of the cortex. In the opinion of the authors these data contradict the concept of the exclusive dependence of the reaction of desynchronization of the encephalogram to the activation of the reticular formation of the medulla oblongata.

The speakers pointed out that the nuclei of the nonspecific system of the optic thalamus and the reticular formation of the medulla oblongata exhibit different reactions to the undonditioned and conditioned alimentary and defensive stimulations.

L. G. Trofimov severely criticized the attempts of a number of foreign investigators at the localization of the processes of closing of the conditional reflex connection in the reticular formation.

In A. I. Shumilina's communication data were adduced on the relative evaluation of the electrical activity of the cortex of the cerebral hemispheres and of the reticular structures of the oblongata, the thalamus, and the hypothalamus upon the production of conditioned inhibition.

The experiments were conducted with rabbits with permanently inserted electrodes. In the course of the experiments it was discovered that upon an increase in the frequency of the conditioned defensive reactions the electrical activity of the cortex and reticular structures of the subcortical formations passes into the synchronized state in the form of slow waves of high amplitude which alternate with flareups of nuclear spindles. The speaker showed that the transition to the stable synchronization includes three stages of variations of electrical activity. The first stage is characterized by the appearance of stable synchronization only in the intervals between the signals. The action of the conditioned stimulus still causes changes in the E.E.G. (electroencephalogram) activity which is specific to the defensive formations, namely, the desynchronization in the senso-motor zone of the cortex and the adjusted rhythm (4-7 per second) in reticular structures of

the subcortical formation investigated. In the second stage of the increase in frequency the synchronization of the electrical activity is manifested even at the moment of application of the higher-frequency conditioned stimulus.

High-frequency oscillations in the senso-motor zone of the cortex which are caused by this stimulus are replaced during the period of action of the conditioned stimulus by slow oscillations which approach the rhythm of the reticular structures, and toward the end of its action pass into the electrical activity of rest. The principal symptom of the third stage of extinction is the absence of desynchronization in the senso-motor zone and the coordinated rhythm in reticular structures of subcortical formations both in the intersignal intervals and during the time of the application of the extinguishing conditioned stimulus. Instead, during the action of the latter, delta waves appear and flareups of the nuclear spindles become more frequent.

A large group of papers was devoted to the study of the changes of the higher nervous activity connected with the effect of aminazine (chlorpromazine) on the ascending reticular activating system. I. A. Zachinyayeva (Moscow) in her paper exposed data on the electroencephalographic character of the formation of conditioned gastroileac positive and inhibiting conditioned reflexes in dogs during continuous application of aminazine. The materials adduced by the speaker indicate that in blocking selectively the adrenergic substratum of the reticular formation aminazine eliminates the conflicting states connected with the development of negative emotions which arise as a result of the nonsupport of the alimentary conditioned reflexes. At the same time the speaker is of the opinion that the ability of the cerebral cortex to produce conditioned gastroileac reflexes during continuous application of aminazine is not disturbed.

Data on the changes in the higher nervous activity of man caused by depression of the ascending activating systems of the brain by aminazine were presented by Prof N. N. Traugott and her associates (Leningrad). On the basis of facts adduced in the paper N. N. Traugott draws the conclusion that depression of the ascending reticular activating system of the medulla oblongata with aminazine depresses the overall tone of the cortex, although it does not affect the closing function of the cortex of the cerebral hemispheres. This is manifested by a change in the effector structure of the reflex, a decrease in the irradiation of the nervous processes, and a depression of the function of the conservation of traces. According to the speaker's data various types of active inhibition change in different ways. The differentiation and the conditioned inhibitor are not affected adversely because of this dissimilarity, whereas trace and lagging reflexes which apparently depend on the tone of the cortical cells are disturbed.

Prof D. M. Gedevarshvili (Tbilisi) and N. A. Kostenetskaya (Leningrad) also reported on the peculiar properties of the effect of aminazine on the higher nervous activity. The paper by V. V. Shidlovskiy (Moscow) exposed a number of fine specific features of the participation of the reticular formation in the formation of vegetative components of the conditioned reflex.

5. Adrenalin, the Sympathetic Tonus, and the Reticular Formation

The session was opened by a large introductory discourse titled "Adrenalin and the Reticular Formation", by Prof A. V. Tonkikh (Leningrad).

The speaker began by discussing the thesis that, according to the opinion established in world literature, the result of the effect of adrenalin on the reticular formation is the reaction of activation of the electrical activity of the cortex of the cerebral hemispheres. In her rejoinder against this one-sided appraisal of the action of adrenalin A. V. Tonkikh pointed to the fact that one of the results of its action on the reticular formation is the secretion of various hormones which exercise different effects on the cortex of the cerebral hemispheres. According to the data of A. V. Tonkikh's laboratory a two-phase action of adrenalin is observed: The first phase, 10-15 minutes after the introduction, is the phenomenon of stimulation which continues approximately one hour is accompanied by desynchronization of the E.E.G. and followed by an abatement and the second phase, drowsiness which passes into deep sleep lasting 4-6 hours. The second phase is accompanied by the appearance of slow electrical waves of high amplitude both in the cortex and in the subcortex. Upon hypophysectomy or cutting of the peduncle of the hypophysis adrenalin does not produce either sleep or any changes in the E.E.G., which fact points to the participation of the hypophysis in the development of sleep upon the secretion of adrenalin.

In the concluding section of her paper Prof A. V. Tonkikh expressed a number of deductions on the relationship between the reticular formation and the central formations of the sympathetic innervation in the diencephalon, the "sympathetic centers," and the role of adrenalin in the adaptional-trophic effect of the sympathetic nervous system.

Great interest was aroused among the listeners by the lecture of A. Ya. Mogilevskiy from Prof A. M. Utevskiy's laboratory (Khar'kov). The speaker presented data on the nature and localization of catecholamines in functionally dissimilar areas of the brain of dogs and adduced certain physiological characteristics of the action of catecholamines on the functionally different divisions of the brain. The chart of the distribution of catecholamines in various divisions of the brain demonstrated by the speaker is more complete than the chart published by the English investigatrix M. Fogt (1954). As it is well known, M. Fogt showed the distribution of adrenaline-like matters mainly in the medulla oblongata and hypothalamus only. Investigations performed by A. Ya. Mogilevskiy show that catecholamines are also contained in a number of nonspecific structures of the thalamus, the rhinencephalon, the "limbicheskiy" [sic] and temporal areas of the cortex, in addition to the already well known exceptionally great concentration of these substances in the medulla oblongata.

A lively exchange during the discussion was precipitated by the paper of Prof A. I. Karamyan (Leningrad) "On the Systems Controlling the Functions of the Higher Orders of the Central Nervous System."

This lecture reported the investigations which indicate that subsequent to the simultaneous removal of the superior and inferior

cervical sympathetic ganglions the weakening or the disappearance of slow oscillations in the cortical E.E.G. is accompanied by the appearance of high-amplitude slow oscillations in the hypothalamus. The introduction of adrenalin in these instances resulted in short-period normalization of the E.E.G. activity in the cortex and the hypothalamus. The destruction of a number of formations in the diencephalon of pigeons produced an effect similar to sympathectomy. However, if the destructions were localized in the dorsal portions of the midbrain, the high-amplitude slow oscillations were observed in the E.E.G. It was also established that the stimulation of the cervical sympathetic nerve produces either strengthening or weakening of the "involving reaction." The introduction of adrenalin produced an analogous effect. A. I. Karamyan holds that the facts adduced in the lecture and other facts known from the literature indicate that the principle of the specific and nonspecific systems reflects only an individual form of the theory of Pavlov, Gaskell, and Orbeli on two forms of nervous activity, namely, the functional and the adaptional-trophic. Precisely because of this A. I. Karamyan believes that there is no basis for reducing the entire activating role of the subcortical formations to the reticular formation only.

In the paper by G. N. Kassil' and L. P. Latash (Moscow) interesting material was presented on the state of the reticular formation upon the introduction into the human organism of small doses of adrenalin and in correlating these doses with certain humoral displacements. A. V. Nasedkin (P. K. Anokhin's laboratory) reported on the effect of chronic action of aminazine on the content of adrenalin-like substances in the brain of the rabbit in embryogeny and Ye. N. Guseva (Kuybyshev) adduced data on the immediate sensitivity of the brain to certain chemical compounds.

6. The Interior of the Organism, Interoception and Their Relationship to the Reticular Formation

At this session a number of problems on the relationship of the interior of the organism with the reticular formation were lectured upon and discussed.

In the paper by Prof A. N. Bakuradze (Tbilisi) a great amount of material was presented on the significance of the reticular formation in the control of vegetative function. In his experiments the electrical activity of various divisions of the brain was studied along with the conditioned and nonconditioned salivary reflexes, the secretion of gastric glands, the pressor and depressor vascular reflexes and the effect thereon of various pharmacological substances. On the basis of the analysis of the factual material reported, Prof A. N. Bakuradze concludes that the reticular formation of the brain produces either a facilitating or an inhibiting effect on the course of the vegetative reactions in the organism.

In the papers of K. M. Kullanda (Moscow) and N. V. Bratus' (Vinnitsa) based on the fine electrophysiological analysis (by the method

of induced potentials) data were presented on the relationship of the reticular formation of the medulla oblongata with the cortex of the cerebral hemispheres and the cerebellum of the afferent systems of internal organs. In particular, K. M. Kullanda presented new facts on the development of original bioelectric reactions arising in the cerebral cortex upon stimulation of certain afferent visceral nerves the second and fourth components of which are connected, in her opinion, to the stimulation of individual groups of neurons in the reticular formation of the medulla oblongata.

I. V. Orlov (Moscow) reported on the participation of the reticular formation of the medulla oblongata and the thalamus in the conduction of afferent impulses from the interoceptors of the uterus.

The papers of Yu. N. Ivanov, G. N. Okuneva (Kuybyshev) and I. S. Repin (Leningrad) were devoted to the effect of humoral respiratory irritants on the functions of the reticular formation to humoral respiratory irritants is incorrect due to the fact that in a number of investigations inadequate amounts of irritants (10% CO₂) were employed and no comparative data were presented. The speakers hold that the preceding investigations of a number of authors point to a stable and not to a high excitability of the reticular formation. In their opinion the existence of a higher sensitivity of hemoreceptors and cerebral cortex to the action of humoral respiratory irritants was overlooked owing to the fact that they are easily injured.

In the paper by I. S. Repin data were adduced on the profound and singular inhibition of E.E.G. by hypercapnia on the basis of which he draws a conclusion that the action of CO₂ on the higher divisions of the brain is direct and inhibiting and that the variations in E.E.G. observed by him are independent of the activating effects of the reticular formation of the medulla oblongata. The interesting and well argued communication of V. M. Khayutin (Moscow) was devoted to the role of the bulbar reticular formation in the reflector control of vessels.

7. Clinical and Experimental Pathology and Reticular Formation

The session was opened by the introductory report of the associate member of the Academy of Medical Science of the USSR Prof P. M. Saradzhishvili (Tbilisi) titled "Certain Endeavors at the Study of Clinical Phenomenology of the Pathology of the Medulla Oblongata on the Basis of Data on the Reticular Formation."

The speaker discussed the selection of the group of symptoms or syndromes which could be attributed to the depression of the reticular formation of the oblongata in the pathological process, taking into account the extreme difficulty of the clinical exposure of the disturbance of the apparatuses of the oblongata and the hypothalamo-diencephalon. In his opinion, we can admit the existence of three basic clinical syndromes connected with the affection of the reticular formation in three different combinations: (a) disturbance of consciousness ("wakefulness"),

(b) dystonic phenomena, (c) vegetative-humoral displacements.

In this direction P. M. Saradzhishvili and his associates are working on the problems of the disturbance of cerebral blood circulation and of the so-called compression epilepsy. As evidenced by the systematic combined clinical and laboratory investigation of these two groups of patients, the majority of cases manifests some stage of inclusion of the reticular formation of the medulla oblongata in the process, and is accompanied by one of the combinations of the three clinical syndromes indicated above. By the application of aminazine and novocaine block of the synocarotid zone as agents affecting the functional state of the reticular formation we can, in the speaker's opinion, facilitate to a certain degree the uncovering of the pathology of the reticular formation of the medulla oblongata.

Interesting data on the effect of afferent impulsation on the medullar formations of the brain and in particular on the reticular formation in children afflicted with cerebral palsy were presented in the communication of K. S. Semenova (Moscow). According to her data, during certain forms of infantile cerebral palsy one of the main symptoms of the affliction is the generalized reaction (defense reaction) to any sudden stimulus. It consists of an abrupt increase in muscular tonus, appearance and increase of chaotic athetotic movements and in the increase of a number of vegetative reactions. The speaker assumes that such a "defense reaction" is connected with the stimulated state of the reticular formation of the medulla oblongata. K. A. Seménova expressed an assumption that in the pathogeny of infantile cerebral palsies great importance must be attached to the immaturity and functional deficiency of the motor system in connection with the disorder of the ontogenic development and the well expressed activity of the medullar divisions of the reticular formation and its constant "facilitating effect" on the pyramidal tracts.

The paper by I. P. Anokhina-Tskova (Moscow) contained a clinical and experimental-physiological analysis of the significance of the change in the state of the reticular formation in patients afflicted with reactive stupor. The speaker pointed out that the principal purpose of the investigation was the examination of the state of the reticular formation during the most profound reactive psychoses, i.e., prestupor and stupor, and the significance of the disorder of the reticular formation function in the inauguration of the clinical picture of these two forms.

In all patients which were in the state of profound stupor of hysterical origin the electrical activity of the brain was characterized by a picture of low-voltage, high-frequency oscillations in all the abductions of the E.E.G. The E.E.G. of patients in the prestupor state was also characterized by high-frequency oscillations but with isolated inclusions of weakly expressed α -rhythm. After the introduction of adrenalin which, as it is well known, stimulates certain apparatuses of the reticular formation, the E.E.G. did not change in spite of the clearly expressed clinical reaction in the form of an abrupt increase in the frequency of the pulse and respiration, paleness, and trembling.

Conversely, upon the introduction of aminazine which blocks the adrenergic apparatuses of the reticular formation the E.E.G. of the patients changed abruptly. A distinct α -rhythm appeared, the reaction to light and sound was registered in the form of desynchronization.

On the basis of the fact that the E.E.G. of the patients in hysterical stupor is characterized by desynchronized oscillations in all abductions of the E.E.G. without any reaction to light and sound, the speaker assumes that the activating apparatus of the reticular formation in these instances is in a high state of stimulation. This is also verified by the fact that adrenalin which stimulates the reticular formation, does not bring about any changes in the E.E.G., whereas aminazine which inhibits the activity of the adrenergic structures of the reticular formation brings about the normalization of the E.E.G. In the opinion of I. P. Anokhina-Tskova this permits us to assume that it is mainly the adrenergic portion of the reticular formation which is in the state of strong stimulation. Clinical data and conclusions drawn on the basis thereof were verified by experiments on rabbits by direct stimulation of the reticular formation.

The communications of Ye. A. Gromova and her associates (Moscow), V. N. Popov and A. N. Razumeyev (Leningrad) were devoted to the significance of the reticular formation in the development of experimental pathological processes.

Ye. A. Gromova reported the experimental data on the significance of the reticular formation of the medulla oblongata in the pathogeny of experimental tetanus. Upon investigating the electrical activity of different divisions of the brain and the biopotential of the muscles, stimulating the reticular formation directly, and introducing aminazine into the experimental animals at various stages of tetanic intoxication, S. A. Gromova notes the participation of the reticular formation in the establishment of the syndrome of tetanus. The speaker believes that in connection with the application of chlorpromazine and aminazine in tetanus therapy in people the data obtained can present a practical interest for treatment of infectious diseases.

8. Symposium of Directors of Laboratories

Toward the end of the conference a symposium was held by all the directors of laboratories present at the conference, who were working on the development of the problems of the cortical-subcortical relationships and, in particular, of the reticular formation of the brain.

Opening the session of the symposium the director of the Institute of Normal and Pathological Physiology of the Academy of Medical Sciences USSR, Prof V. V. Parin noted that at the present time it is necessary to review the results of scientific investigation of the problems of the reticular formation in the laboratories of the Soviet Union and to plan the pathways of future scientific investigations. He emphasized the fact that during the recent years the scope of scientific operations on the study of the cortical-subcortical relationships has been appreciably

expanded and a number of new laboratories were included in the work. In connection with this it is especially important that a single point of view be developed by the directors of scientific collectives and laboratories so that in the future the study of these problems may be conducted purposefully and jointly.

Next, Prof P. K. Anokhin delivered a communication on the ways and prospects of further development of the problems of the reticular formation and the system of the interrelationships of cerebral cortex and subcortical formations.

The speaker dwelt on the problems of the combined approach in the study of the reticular formation of the brain. The experience of the present conference shows that only the joint efforts of morphologists, physiologists, pharmacologists, and clinicians would render feasible the approach to a correct and omnilateral concept of the role and place of the reticular formation in the complex system of cortical-subcortical relationships, deciphering and comprehending the "blind force of the subcortex" (I. P. Pavlov) which it exercises on the cortex of the cerebral hemispheres and the way in which the cerebral cortex brings about the controlling and regulating effect on the functions of the subcortical apparatuses. In this connection it is especially important that the efforts of the various laboratories working on this problem be united, that an actual consulting assistance to the young and provincial scientific collectives be provided and that a purposeful, broad program of investigations be established.

The second question raised in the address concerned the necessity of the study of the problems of the reticular formation in the closest and methodical contact with the doctrine of I. P. Pavlov on the higher nervous activity.

The speaker noted that unfortunately during the recent times one often hears of the existence of a "science" of the reticular formation. In his opinion a "science" of the reticular formation never existed and does not exist and there is only a division of neurophysiology which has been rapidly developing in the recent years and is extremely important for understanding the role of the mechanics of the cortical-subcortical relationships in the integrating activity of the brain.

The third problem which had been posed in the principal paper concerned the utilization of the gigantic amount of scientific heritage of the school of N. Ye. Vvedenskiy and A. A. Ukhtomskiy. The speaker emphasized that at the present time it has become obvious that, for example, it is impossible to comprehend the way in which the reticular formation exercises an ascending activating effect unless we employ the system of analysis on the basis of the doctrine of Vvedenskiy and Ukhtomskiy on the lability of the parabiosis.

The fourth topic concerned the relationship between the nonspecific effects of the reticular formation and the adaptional-trophic action of the sympathetic nervous system studied by the school of L. A. Orbeli. In P. K. Anokhin's opinion it is necessary that this relationship be thoroughly investigated, whereby a number of important mechanisms in the activity of the brain may be disclosed.

The fifth and last topic discussed by the speaker was devoted to the relationship between the psychiatric and neuropathological clinical treatment in the study of the problems of physiology and pathology of the reticular formation. Even now in many of the papers heard at the present conference the transition to the problems of clinical pathology became apparent. However, in the opinion of the speaker, this contact is as yet poorly developed. At the same time both the theoreticians and clinicians have much to gain from the development of the contacts and investigation of the cortical-subcortical relationships by experimentation and in clinical practice.

The speaker dwelt in detail on two problems: (1) the study of the controlling and regulating effect of the cortex of the cerebral hemispheres on the activity of the reticular formation and other subcortical structures during the closing of the temporary connection and (2) on the further development of the investigation of the neurochemical sensitivity of the reticular neurons taking into consideration many specific features and their physiological, morphological, and biological characteristics.

In conclusion the speaker emphasized the fact that the investigation of the functions and relationships of the reticular formation must be conducted within the general system of the study of the cortical-subcortical relationships on the basis of the extremely rich scientific heritage of I. M. Sechenov, V. M. Bekhterev, I. A. Pavlov, N. Ye. Vvedenskiy, and A. A. Ukhtomskiy.

Thereupon began the discussion of the general and specific neurophysiological problems posed during the conference.

In opening the discussion Prof A. I. Smirnov dwelt on the examination of a number of neurophysiological problems and shared with those present the results of the many years' investigations in his laboratory of the participation and significance of the respiratory center in maintaining the general tonus of excitability of the cortex of the cerebral hemispheres.

L. G. Trofimov stated that in his opinion the introductory papers read during the plenary session of the conference and, in particular, P. K. Anokhin's paper, should have contained an analysis of the present state of the study of physiology of the reticular formation and especially of its significance in closing the conditioned-reflex connections on the basis of the works of the Soviet and foreign scientists, and that less should have been said of the work of their laboratories. The same idea was expressed by Prof I. A. Arshavskiy in his speech. Subsequently, L. G. Trofimov examined a number of general problems of the theory of electroencephalography in relation to the study of the activating effects of the reticular formation.

A number of important questions was raised in the address by G. D. Smirnov. First of all G. D. Smirnov pointed to the fact that, in his opinion, at the present time there exists a mass enthusiasm for the problems of the reticular formation which might divert the attention of the investigators from a profound study of the specific features of

various divisions of the central nervous system and the cerebral cortex. He concurred in the idea expressed by the speaker that the study of the reticular formation must be conducted within a common plan of investigation of the cortical-subcortical relationships. Thereupon G. D. Smirnov noted the necessity of a still greater development of modern precise methods of physiological analysis in our laboratories. He made a number of general observations with respect to the further development of the investigations of the reticular formation in three directions: (1) a broad general biological approach to the integrative activity of the brain on the basis of the method of conditioned reflexes, (2) the study of the relay functions of the reticular formation ensuing from the morphological investigations, and (3) the chemical heterogeneity of the reticular formation.

In conclusion, he dwelt on the criticism of the concepts presented by the well known Canadian neurosurgeon U. Penfield on the localization of the consciousness in the reticular formation. G. D. Smirnov emphasized that from personal conversations with Prof Penfield and upon reading his latest publications he formed an impression that Penfield has modified somewhat his point of view and his previous concepts of the step-by-step structure of the nervous system and of the centrencephalic theory of consciousness.

S. A. Sarkisov's communication was comprehensive and interesting. He concurred in the opinion of the speaker on the group approach to the study of the functions of the reticular formation.

The second important question to which S. A. Sarkisov called the attention of the audience concerned the heterogeneity of the structure of the reticular formation. He believes that we cannot speak of the reticular formation in general but that we must speak of specific structures and connections between the subcortical formations and between these formations and the cortex of the cerebral hemispheres and that the entire subcortex cannot be reduced to the reticular formation only. Thereupon he dwelt on the problem of the relationship between specific and nonspecific formations to which a conference in the Cerebral Institute of the Academy of Medical Science USSR was devoted. The greater portion of S. A. Sarkisov's communication concerned the necessity of a serious scientific criticism of antimaterialistic views of the modern foreign physiologists. A similar idea of the necessity of the development of criticism against the distortions of the bourgeois science was expressed in the communications of M. Ya. Rabinovich and O. S. Adrianov. The latter spoke of the necessity of the defense of the supremacy of the leading figures of the home physiology in the study of the cortex-subcortex relationship.

N. V. Golikov dwelt on the examination of a series of neurophysiological problems connected with the further study of the physiological functions of the reticular formation. He outlined five principal directions for future investigations: (1) Participation and significance of the reticular formation in the systemic reactions of neurocenters; (2) the nature of the specific effect of the reticular formation on the

functional state and polarization level of cortical cells; (3) adrenergic and cholenergic components of the reticular formation in the central nervous system during prolonged changes in the level of excitability of the reticular formation; (5) trace processes in the reticular formation and cerebral cortex when these divisions of the brain are in various physiological states. He did not share the misgivings expressed by G. D. Smirnov concerning the broad attention given to the problems of the reticular formation. To the contrary, in his opinion, a broad development of the problem had been beneficial and even now it is possible to plan specific pathways for the investigations of a number of important and crucial problems connected with reticular formation.

A. I. Karamyan invited the attention of the audience to a number of important problems. First of all he suggested that it is necessary to study the evolution of the functions of reticular formation on a broad physiological plan. Then he dwelt on the general theory of electroencephalography and on the necessity of an explanation of the intimate nature of processes concealed behind the terms: "desynchronization" and "synchronization." In the second portion of his speech A. I. Karamyan spoke of the significance of the sympathetic nervous system in upholding the tonus of the cerebral cortex and of his differences of opinion with P. K. Anokhin on certain experimental problems.

In his address N. G. Kostyuk entirely concurred with the thesis promulgated in the principal discourse on the necessity of group investigations of the activity of subcortical formations. According to P. K. Kostyuk the study of the cellular mechanisms in the activity of the corresponding subcortical structures must be assigned an important place in the combined group effort.

Ye. A. Gromova did not share the misgivings on the expediency of the assembling of such large group conferences as the present one. In her opinion the great interest aroused by the conference and the discussion of problems at the symposium will contribute to the correct orientation of the great army of physiologists toward the solution of the central and crucial problems of the reticular formation in the general system of the relationship between the cerebral cortex and the subcortical structures. Thereupon Ye. A. Gromova dwelt in detail on the characterization of the participation of the reticular formation in the explanation of the general mechanisms of the development of pathological processes.

She believes that the present-day knowledge of the various functions of the reticular formation provide a new serious scientific basis for the A. D. Speranskiy's concepts of nervous trophic system.

In G. N. Kassil's communication a question concerning the mechanics of humoral activation of the reticular formation was raised. He remarked on the great significance of the hematoencephalic barrier in the study of the action of such substances as adrenalin on the central nervous system and adduced examples of different effects produced by this substance when introduced intravenously or into the ventricles of the brain.

G. N. Kryzhanovskiy proposed that the audience think on the definition of the concept of the reticular formation which would include morphological, physiological, and biological characteristics of this vast area of the central nervous system. He cautioned against the revaluation of the fine analytical methods of investigation of the functions of subcortical formations and concurred in the previously expressed desire for a timely reaction against all attempts of foreign scientists at the corruption of the basic principles of the importance of the cortex of cerebral hemispheres in the formation and origination of temporary connections. G. N. Kryzhanovskiy proposed to convoke similar conferences and symposiums for the study of reticular formation once every two years.

The greater portion of the discourse by S. P. Narikashvili was devoted to the analysis of the problems of cortical control of the activity of nonspecific systems of the brain and of the regulation of the influx of the stream of afferent impulses into the central nervous system.

A. V. Tonkikh stressed the participation and importance of the doctrine of L. A. Orbeli on the adaption-trophic influence of the sympathetic nervous system in the activity of the cerebral cortex. She called on the audience not to forget the experiments of L. A. Orbeli and his disciples in this area of physiology of the central nervous system and to utilize these achievements in the study of the cortical-subcortical relationships, and particularly, of the reticular formation.

P. M. Saradzhashvili dwelt on the significance of the reticular formation in clinical pathology of the brain. He spoke in favor of the development of joint investigations of the mechanisms of cortical-subcortical control in clinical and experimental work. After speeches of A. V. Val'dman and L. S. Gambaryan the concluding speech was delivered by P. K. Anokhin.

In summarizing the transactions of the symposium V. V. Parin analyzed in detail the principal desires and ideas expressed by the participants of the discussion. He appealed to the scientists to continue the interesting investigations which are conducted in their laboratories and in their subsequent work to take into account the principal remarks and recommendations made at the symposium.

The symposium recommended to conduct further study of the reticular formation according to a number of the following general directions:

- (1) The study of the precise physiological regularity in the nature of the activating effect of the reticular formation on the cerebral cortex in the system of constellations of the subcortical centers.
- (2) A detailed characteristic of the specific morphological, physiological and pharmacological features of the structures and functioning of the neurons of the reticular formation.
- (3) Examination of the specific morpho-physiological features of the interaction of the specific and nonspecific afferent brain systems.
- (4) The controlling effect of the cortex of the cerebral hemispheres on the afferent and efferent functions of the reticular formation.

(5) The participation and the position of the reticular formation in the series of other subcortical structures during the closing of the temporary connections.

(6) Specific features of the descending effects of the reticular formation on the activity of the spinal cord.

(7) Interaction of the medullar and thalamic nonspecific systems.

(8) Specific features of the development of the structure and function of the reticular formation in phylo- and ontogeny.

(9) The participation of the reticular formation in the accomplishment of the adaption-trophic effects of the sympathetic nervous system.

(10) Specific features of the participation of the cerebral cortex and the nonspecific systems in the regulation of the inflow of the current of afferent stimulations along the specific conducting tracts in the process of "habituation."

(11) The participation and significance of the reticular formation in the development and pathogeny of experimental and clinical afflictions of the central nervous system.

A decision was accepted on the systematic convocation of similar combined conferences and symposiums on the problems of reticular formation once every two years.

The papers read at the conference and the speeches delivered at the symposium showed that the Soviet physiologists solve these problems not from the position of a narrow analytical method which is characteristic of the great majority of the foreign investigators but by developing them in the broad general-biological plan of the entire organism and its relationships with the external and internal media.

The symposium of the directors of laboratories emphasized the fact that in spite of the great significance of the study of the problems of reticular formation, its development must not proceed separately from the investigations of other subcortical structures and the controlling position of the cerebral cortex and should be performed only on the basis of the Marxist-Leninist philosophy and the best materialistic traditions of the classics of Russian and Soviet physiology.